

AD_____

GRANT NUMBER DAMD17-98-1-8349

TITLE: ETACT - An Innovative Approach to Scintimammography

PRINCIPAL INVESTIGATOR: Frederic H. Fahey, D.Sc.

CONTRACTING ORGANIZATION: Wake Forest University School of Medicine
Winston-Sale, North Carolina 27157-1088

REPORT DATE: July 1999

TYPE OF REPORT: Annual

PREPARED FOR:

U.S. Army Medical Research and Materiel Command
Fort Detrick, Maryland 21702-5012

DISTRIBUTION STATEMENT: Approved for Public Release;
Distribution Unlimited

The views, opinions and/or findings contained in this report are those of the author(s) and should not be construed as an official Department of the Army position, policy or decision unless so designated by other documentation.

REPORT DOCUMENTATION PAGE

Form Approved
OMB No. 0704-0188

Public reporting burden for this collection of information is estimated to average 1 hour per response, including the time for reviewing instructions, searching existing data sources, gathering and maintaining the data needed, and completing and reviewing the collection of information. Send comments regarding this burden estimate or any other aspect of this collection of information, including suggestions for reducing this burden, to Washington Headquarters Services, Directorate for Information Operations and Reports, 1215 Jefferson Davis Highway, Suite 1204, Arlington, VA 22202-4302, and to the Office of Management and Budget, Paperwork Reduction Project (0704-0188), Washington, DC 20503.

1. AGENCY USE ONLY (Leave blank)

2. REPORT DATE
July 1999

3. REPORT TYPE AND DATES COVERED
Annual (1 Jul 98 - 30 Jun 99)

4. TITLE AND SUBTITLE
ETACT- An Innovative Approach to Scintimammography

5. FUNDING NUMBERS
DAMD17-98-1-8349

6. AUTHOR(S)
Frederic H. Fahey, D.Sc.

7. PERFORMING ORGANIZATION NAME(S) AND ADDRESS(ES)
Wake Forest University School of Medicine
Winston-Sale, North Carolina 27157-1088

8. PERFORMING ORGANIZATION
REPORT NUMBER

9. SPONSORING / MONITORING AGENCY NAME(S) AND ADDRESS(ES)
U.S. Army Medical Research and Materiel Command
Fort Detrick, Maryland 21702-5012

10. SPONSORING / MONITORING
AGENCY REPORT NUMBER

11. SUPPLEMENTARY NOTES

12a. DISTRIBUTION / AVAILABILITY STATEMENT
Approved for Public Release; Distribution Unlimited

12b. DISTRIBUTION CODE

13. ABSTRACT (Maximum 200 words)

This project investigates the use of a novel approach to scintimammography (SMM) known as emission tuned aperture computed tomography (ETACT). In ETACT, a series of projections of the radionuclide distribution in the breast are acquired with fiducial markers. These data are reconstructed into tomographic slices. The hypothesis of this project is that ETACT will significantly increase the diagnosis accuracy of SMM, and can be applied in a simple, flexible and practical manner. We have developed a simulation model for the acquisition process of ETACT and have used this tool to perform a preliminary evaluation of the aperture size appropriate for ETACT. It was determined that a 4 mm diameter aperture was optimal for ETACT, as currently implemented. We performed a preliminary phantom evaluation to compare its performance to planar SMM. This evaluation indicated that contrast (0.2 vs 0.52) and the SNR (0.54 vs 2.05) were substantially higher for ETACT as compared to planar SMM. We will continue to work on our ETACT simulator to include attenuation and scatter. We will simulate ETACT data to evaluate aperture size and projection divergence as a function of tumor size, location and T/NT ratio. We will develop a methodology for acquiring ETACT data using optical markers. We will acquire phantom data to evaluate fiducial placement, tumor size and location, the effect of cardiac or liver activity and compare the results to SMM. In the third year, we will continue to evaluate ETACT and develop an ETACT clinical prototype.

14. SUBJECT TERMS
Breast Cancer

Scintimammography, nuclear medicine, SPECT, tomography,

15. NUMBER OF PAGES
26

16. PRICE CODE

17. SECURITY CLASSIFICATION
OF REPORT
Unclassified

18. SECURITY CLASSIFICATION
OF THIS PAGE
Unclassified

19. SECURITY CLASSIFICATION
OF ABSTRACT
Unclassified

20. LIMITATION OF ABSTRACT
Unlimited

FOREWORD

Opinions, interpretations, conclusions and recommendations are those of the author and are not necessarily endorsed by the U.S. Army.

_____ Where copyrighted material is quoted, permission has been obtained to use such material.

_____ Where material from documents designated for limited distribution is quoted, permission has been obtained to use the material.

PP Citations of commercial organizations and trade names in this report do not constitute an official Department of Army endorsement or approval of the products or services of these organizations.

_____ In conducting research using animals, the investigator(s) adhered to the "Guide for the Care and Use of Laboratory Animals," prepared by the Committee on Care and use of Laboratory Animals of the Institute of Laboratory Resources, national Research Council (NIH Publication No. 86-23, Revised 1985).

_____ For the protection of human subjects, the investigator(s) adhered to policies of applicable Federal Law 45 CFR 46.

_____ In conducting research utilizing recombinant DNA technology, the investigator(s) adhered to current guidelines promulgated by the National Institutes of Health.

_____ In the conduct of research utilizing recombinant DNA, the investigator(s) adhered to the NIH Guidelines for Research Involving Recombinant DNA Molecules.

_____ In the conduct of research involving hazardous organisms, the investigator(s) adhered to the CDC-NIH Guide for Biosafety in Microbiological and Biomedical Laboratories.

 7/31/99
PI - Signature Date

Table Of Contents

1. Front Cover	1
2. Standard Form 298.....	2
3. Foreword.....	3
4. Table of Contents.....	4
5. Introduction	5
6. Body of Report	6
7. Key Research Accomplishments	14
8. Reportable Outcomes	15
9. Conclusions	16
10. References	17
11. Appendices	18

Introduction

This project is investigating the use of a novel approach to scintimammography (SMM) known as emission tuned aperture computed tomography (ETACT). ETACT is based on the more general tuned aperture computed tomography (TACT) method used in radiography. TACT has been successfully applied in dentistry and its use in conventional mammography is currently being investigated. In ETACT, fiducial markers are placed around the object being imaged. A series of projection images are then acquired using a standard gamma camera with a pinhole (or other) collimator from any angle and at any distance, as long as all of the markers are within the field of view. The data are then reconstructed into a series of tomographic slices. This can be reconstructed easily on a PC. Thus TACT requires no expensive, dedicated hardware. The beauty of this approach is that, if successful, this method could be applied in practically every hospital in the US, almost immediately. The main hypothesis of this project is that the application of ETACT will significantly increase the diagnostic and prognostic accuracy of SMM, particularly for small, nonpalpable lesions, and that this innovative method can be applied in the clinic in a simple, flexible and practical manner. The specific aims of this research are as follows:

1. to develop and utilize a computer simulation model of ETACT to determine the optimal parameters for its application and to compare it to conventional SMM,
2. to utilize phantom data to further compare ETACT to conventional SMM, both planar and SPECT, and
3. to design a clinical ETACT prototype system that will then be used in a subsequent preliminary clinical investigation.

In this report, we will present our progress in the development of a computer simulation model of ETACT, the preliminary results from the use of such a model, and some preliminary phantom experiment results. We will discuss the changes in our approach that has been dictated by these preliminary results and present an outline for the remainder of this project.

Body of the Report

I. ETACT

In ETACT, one or more fiducial markers are placed about the patient's breast. A series of projection images are then acquired with a pinhole-collimated, gamma camera. We use pinhole collimation for three reasons. First, pinhole collimators are routinely available for most portable, gamma cameras, making this method a straightforward approach that can be applied in practically any hospital. Secondly, we plan to take advantage of the high resolution associated with pinhole collimation. For a typical pinhole collimator of length of 30 cm and pinhole diameter of 4 mm as well as an intrinsic spatial resolution of the detector of 3.5 mm, the system spatial resolution is approximately 5 mm compared to that of planar and SPECT imaging with a high resolution collimator of approximately 7 mm and 10 mm, respectively. Special inserts could also be made that would reduce the pinhole diameter from 4 to 2 mm improving the resolution to approximately 3 mm. Thirdly, the collimator sensitivity is inversely proportional to the square of the aperture-to-object distance whereas the sensitivity of a parallel hole collimator does not vary with collimator-to-object distance.

Consider the technique known as "tomosynthesis" (Grant 1972). In this case, the detector (the gamma camera crystal) is always oriented parallel to the tomographic plane of interest. Several projections are acquired such that all of the aperture (pinhole) locations are known, coplanar and parallel to the tomographic plane of interest (figure 1). A series of tomographic planes can be reconstructed by appropriately shifting the projection data and adding them together. All reconstructed planes are parallel to the detector plane. Tomosynthesis has been shown to be a very simple and effective manner of generating tomographic data. However, it places many constraints on the acquired projection data, and the aperture locations for all of the projections must be known.

ETACT alleviates these geometric constraints by using the projected locations of a series of fiducial markers to obtain knowledge concerning each projection (Webber 1997). Consider the case where the detector is still coplanar and parallel to the tomographic plane of interest, but the actual location is not known. A fiducial marker whose location relative to the object is fixed is also imaged within each projection. Consider a reference plane whose location is the same as the aperture to detector distance, but whose location is opposite the detector (see figure 1). If we overlay all of the

projections, determine the center of mass (COM) of the projected locations of the marker, shift all of the data such that projected location of the marker coincides with the COM and add the data together, we would reconstruct the plane that contains the fiducial marker and is parallel to the detector plane. If the projections are shifted by half that amount and added, then the plane that is half way between the marker and the reference plane is reconstructed. In this manner, a series of tomographic planes can be reconstructed.

In the present implementation of ETACT, 5 markers are used, four of which are coplanar and one of which is not. The four coplanar markers are used to transform all of the acquired projections such that they appear to all have been acquired with the aperture in a common plane. The fifth marker is then used as described above to shift and add the projections to reconstruct the series of tomographic slices. It also has been demonstrated that this approach with the five fiducial markers can be used to reconstruct the data even if the detector in each projection is not always in the same plane. In summary, if we acquire a series of projection images using a set of 5 fiducial markers (4 coplanar and one out of plane), we can reconstruct the data into a series of tomographic slices, even if the location of neither the detector nor the aperture is known. It is also not necessary to have the detector in the same plane or at the same distance in each projection. Therefore, ETACT is a simple and flexible method of acquiring and processing tomographic data.

ETACT is a form of “blurring” tomography, that is, the activity that is not in the plane of interest is still present in the image, but it is blurred. Therefore, if there is a lot of out-of-plane activity, the contrast may be substantially blurred. In addition, very “hot” features (i.e. features with much more activity than the background) that are out-of-plane will lead to artifacts in the plane of interest. These artifacts can mimic small tumors in the ETACT images. The axial spatial resolution (i.e., the resolution in the direction normal to the tomographic plane of interest) is determined by the divergence of the acquired projection data. However, even in the best of cases, the axial spatial resolution is quite limited. We are currently investigating two approaches to address both of these limitations. The simplest approach is to apply an iterative deconvolution since we can *a posteriori* determine the point spread function (PSF) of the system. In addition, if we acquire two sets of projections that are basically perpendicular to each other, then we can “merge” the two ETACT reconstructions. In this manner, data that is not consistent with one of the ETACT acquisitions can be removed or at least minimized in the resultant, processed data. We are currently evaluating both of these approaches.

II. Development of the ETACT Simulation Model

In order to investigate a number of the parameters associated with ETACT, we are developing a computerized, simulation model of the acquisition of ETACT data. Due to the three-dimensional (3D) nature of this process, this model is currently being developed using an Silicon Graphics, Inc. (SGI) workstation. It is our plan to migrate this application to Windows NT using the OpenGL libraries. The model currently allows you to define an arbitrary 3D object with a set of markers. The activity associated with each component can be defined. For example, we have defined a breast containing a tumor with 5 markers. The target-to-nontarget (T/NT) ratio of the tumor was 5:1. A projection from this simulated object is shown in Figure 2. In addition, the detector size and aperture-to-detector distance can be defined. Once the detector configuration and the object are defined, the detector can be moved interactively about object and simulated projections obtained. These data can be subsequently reconstructed with the standard, ETACT software. In the simulations processed thus far, the projections were blurred to the resolution and Poisson noise added that were consistent with the aperture size chosen. These will eventually be incorporated into the simulation application as will photon attenuation and scatter. This simulation model will be used to evaluate the acquisition parameters associated with ETACT such as the aperture size, the aperture to object distance, the number of projections and the angular disparity of the projections.

III. Preliminary Evaluation of Aperture Size Through Simulation

We have performed a preliminary evaluation of the required aperture size for ETACT. We modeled the breast as a hemisphere with 15 cm diameter. The tumor was a 1 cm diameter sphere with a 5:1 T/NT ratio. Five markers (4 coplanar and one out-of-plane) were placed lateral to the breast. The detector was modeled as a gamma camera with a 40x40 cm field-of-view. The aperture-to-detector distance was 35 cm. The three aperture sizes used were 3, 4 and 5 mm. The aperture-to-object distance of approximately 25 cm was chosen such that the object, including the markers, took up the majority of the field of view. Using our projection simulator, we constructed 8 noiseless projections for each aperture size. The angular divergence was approximately +/- 20 degrees. One

such projection is shown in Figure 2. Based on the calculated system spatial resolution of each pinhole, the projection data were blurred with a gaussian kernel. Based on the sensitivity of each pinhole size, Poisson noise was added to each pixel. These data were then reconstructed using the standard TACT reconstruction software.

To evaluate these data, the slice through the middle of the tumor was visually selected and a region of interest (ROI) was drawn about the tumor and the maximum pixel value (Max) in the ROI was determined. A similar sized and shaped ROI was placed lateral to the tumor to evaluate the background activity. The mean pixel value (BKG) and the standard deviation (SD_{BKG}) in the background ROI were determined. The contrast (C) was calculated using the formula

$$C = \frac{\text{Max} - \text{BKG}}{\text{BKG}}$$

A detectability index referred to as the SNR was calculated by

$$\text{SNR} = \frac{C}{(SD_{BKG}/\text{BKG})}$$

The results of this investigation are summarized in the table below.

Aperture (mm)	Rel Sens	Res(mm)	C	SNR
3.0	0.56	5.7	0.13	1.92
4.0	1.00	7.2	0.18	2.20
5.0	1.56	8.9	0.12	2.02

The sensitivity is given at the central axis of the collimator and relative to the value for the 4 mm aperture. The resolution is the FWHM (including a 3.5 mm intrinsic resolution of the detector) at the object plane. C and SNR were calculated from the formulae above. In this preliminary investigation, the 4 mm aperture yielded the optimum contrast and signal-to-noise ratio.

IV. Preliminary Phantom Experiment

A preliminary phantom experiment was performed to test the feasibility of the approach and to evaluate the practicality of the approach. We also sought to compare the lesion detectability using ETACT to a conventional planar acquisition. For this experiment, we used the Data Spectrum breast phantom with the 1 cm tumor. For this initial experiment, we wanted to make sure that we could detect the lesion, so we used a 10:1 T/NT ratio. A portable gamma camera with a small field-of-view (30x30 cm) was used with a 4 mm pinhole aperture. The aperture-to-tumor distance was approximately 20 cm. We used 5 markers (4 coplanar and one out of plane) as described earlier. These were point sources consisting of small amounts of Tc-99m placed at the ends of capillary tubes. The Data Spectrum phantom is shown in Figure 3. The tumor can be seen within the breast. The markers are also visible. The 4 coplanar markers are just inside the white balls of the plastic frame and the 5th marker is at the end of the red rod. Eight projections were acquired for 5 minutes each. Four of the eight projections are shown in Figure 4. The 5 markers are clearly visible in these projections. The tumor is subtle and noted by the arrows.

These data were reconstructed into a series of slices using the standard ETACT algorithm as described earlier. Four of these slices are presented in Figure 5. The image in the upper left represents the slice through the marker on the end of the red rod in Figure 4. The upper right represents the slice through the 4 coplanar markers. The lower left is the slice through the middle of the tumor and the lower right is an arbitrary slice through the breast. The tumor is clearly visible in the image in the lower left. The contrast, C, and the SNR as described earlier were determined for ETACT slice and compared to a planar acquisition. The results are shown below.

<u>Method</u>	<u>C</u>	<u>SNR</u>
Planar	0.20	0.54
ETACT	0.52	2.05

As can be seen, the ETACT data demonstrated substantially more contrast in this preliminary evaluation.

V. Summary of Preliminary Evaluation and Future Directions

These studies demonstrate the feasibility of the ETACT approach as well as the potential for improved lesion detectability. They also demonstrated the need to image at a substantial distance (about 25 cm) in order to image the entire object including the markers. Imaging at such a distance leads to a substantial loss in the effectiveness of the pinhole collimator. The sensitivity of the pinhole collimator falls off as the inverse square of the object-to-aperture distance. Therefore, if we could reduce the aperture-to-object distance by a factor of 2, we would see a 4 fold increase in the number of counts and the noise level would decrease by half. Alternatively, we could either reduce the imaging time or improve the spatial resolution by using a smaller aperture size. At the same time, the spatial resolution of the systems dramatically improves with a shorter imaging distance. Figure 6 are graphs of the sensitivity and spatial resolution of a 3 mm pinhole. The advantage of imaging at short distances is evident from this figure.

Two different approaches are perceived for using ETACT in scintimammography. One is imaging the entire breast or axillary region looking for tumors or involved lymph nodes. In this case the entire region would be imaged. For example the entire breast would need to be within the field of view. The other is that a feature has been deemed suspicious according to some other modality (say the mammogram) and we are only interested in imaging that small region to determine whether there is any uptake of the radiotracer. In both of these cases we would like to image at as small a distance as possible. However, currently, we are limited by the necessity of including the markers in each image. If we could devise a method for imaging the markers that did not put the geometric constraints of imaging distance on the system, then we should be able to acquire substantially better data than indicated in our preliminary study. In addition, the markers in the radionuclide image appear very similar to the feature of interest (tumors). Both are small, hot features on the image. If a marker is very hot compared to the tumor, it can make the tumor difficult to discern. This ambiguity can potentially limit the effectiveness of the ETACT approach. If we could utilize a marker system that was not radioactive, it could alleviate this problem.

For these reasons, we are investigating the use of an optical sensor, calibrated to the nuclear imager, for imaging the markers. Our prototype will consist of a digital optical camera that is mounted rigidly to the gamma camera head. A calibration scheme will be developed in order to map the location of the optical markers onto the radionuclide image. The radionuclide projection images

as well as the optical images of the breast will be acquired simultaneously with the gamma camera as close as necessary to image the region of interest. The locations of the optical markers will then be mapped onto the radionuclide projection image space and the ETACT reconstruction algorithm will be applied. We expect that this approach will yield a substantial improvement in image quality and will eliminate the ambiguity introduced by the presence of the markers in the radionuclide image.

VII. Review of Statement of Work

In this section, we will review the original statement of work and review the status of each component. The review on current status for each step will be in square brackets [] and italicized so that it will be easily distinguishable from the original task.

Task 1: To develop and utilize a computer simulation model (Months 1-15) [*new estimate is Months 1-20*]

- Develop female, thoracic computer phantom including breasts, tumor, lymph nodes, heart, liver and lungs [*We have developed a simulated breast and tumor but have not include this in with the rest of the torso. This will be accomplished in Months 13-15*]
- Model radiologic properties of phantom including emission, detection, attenuation, scatter and Poisson noise [*We have modeled emission, detection and Poisson noise. Modeling of attenuation and scatter will be complete in Months 13-18*]
- Model ETACT with number of fiducial markers, placement of markers, number and orientation of ETACT views [*This has been completed*]
- Model conventional SMM including both planar and SPECT [*We have modeled conventional planar imaging. SPECT is straightforward and will be modeled in Months 13-15*]
- Run simulations varying lesion size, location and T/NT ratio [*These simulations will be run in Months 15-18. In addition, aperture size and projection divergence will be evaluated.*]
- Determine SNR and perform ROC analysis to compare different ETACT configurations to each other and to conventional SMM [*This will be done in Months 18-20*]

Task 2: To acquire and utilize phantom data to further compare ETACT to conventional SMM (Months 6-27)

- Develop phantom protocol including lesion placement, size and T/NT ratio and activity in other organs (heart, liver and chest) [*We have acquired the Data Spectrum with torso and liver. We will order the cardiac insert. As stated above, we are also developing an approach using optical markers. This will be done in Months 13-18*]
- Acquire ETACT data with portable gamma camera and pinhole collimator varying number and location of fiducial markers, number and location of views and reconstruction method [*These studies will be done in Months 15-24*]
- Acquire conventional SMM including planar and SPECT [*This will be done in conjunction with the above sub-task in Months 15-24*]

- Perform ROI analysis to determine the SNR in the phantom data [*This will be done in Months 13-18*]
- Perform ROC analysis to compare different implementations of ETACT to each other and to conventional SMM [*This will be done in Months 20-27*]

Task 3: To design a clinical ETACT scintimammographic system prototype (Months 24-36) [*It is expected that Task 3 will be carried out as originally designed*]

- Based on results of Tasks 1 and 2, design the optimal, acquisition parameters for ETACT SMM
- Design a system for reliable and practical method of marker placement
- Review design with both technical and physician staff in both nuclear medicine and mammography
- Modify and finalize design based on clinical feedback

Key Research Accomplishments

Task 1: To develop and utilize a computer simulation model

- We have developed a 3D tool for simulating the ETACT acquisition process including emission, pinhole collimation, detection and Poisson noise.
- We have developed a simple breast tumor model for the evaluation of scintimammography.
- We have performed a preliminary evaluation of the aperture size using the simulation application described above.

Task 2: To acquire and utilize phantom data to further compare ETACT to conventional SMM

- We have acquired the Data Spectrum breast phantom and have developed a protocol for imaging this phantom with fiducial markers using a portable gamma camera with a pinhole collimator.
- We have acquired a preliminary comparison between ETACT and planar SMM using phantom data.

Reportable Outcomes

Fahey FH, Webber RL, Harkness BA. ETACT: a novel approach to scintimammography. J Nucl Med 1998; 39:24P (abstract, presented at the Society of Nuclear Medicine Annual Meeting, Toronto, June 1998)

Fahey FH, Webber RL, Bayram E, Harkness BA, Mu Z, Hemler P. Preliminary Evaluation of ETACT Scintimammography. Med Phys 1999; 26:1072 (abstract, presented at the American Association of Physicists in Medicine Annual Meeting, Nashville, July 1999)

Note: Both of these abstracts are included in the appendix.

Conclusions

We have implemented the ETACT reconstruction algorithm that we described in our application. We have also developed a computerized simulation model for the acquisition process associated with ETACT including emission, collimation, detection and Poisson noise. We have also developed a simple model for the breast with a small tumor which also includes the fiducial markers necessary for doing ETACT. We used these simulation tools to perform a preliminary evaluation of the aperture size appropriate for ETACT. Based on this evaluation, it was determined that a 4 mm diameter aperture was optimal for ETACT, given the use of a portable gamma camera with a pinhole collimator and using radioactive markers. In addition, we obtained the Data Spectrum breast phantom with tumor inserts and developed a technique for creating adequate radioactive fiducial markers and for acquiring pinhole projections of the phantom. Using this phantom, we performed a preliminary evaluation to test the feasibility of this approach and to compare its performance to planar SMM. This evaluation indicated that contrast (0.2 vs 0.52) and the SNR (0.54 vs 2.05) was substantially higher for ETACT as compared to planar SMM. However, both of these evaluations indicated that we need to greatly reduce the aperture-to-object distance if we are to improve the performance of ETACT. In order to accomplish this, we will investigate the use of optical fiducial markers with a digital camera.

In the next year, we will further develop a female, thoracic phantom that includes breasts, tumors, lymph nodes, heart, lungs, and liver. We will continue to work on our ETACT simulator such that it will include tissue attenuation and scatter. We will also migrate this application to work on an NT workstation. We will model conventional SMM as well as SPECT. We will then simulate ETACT projection data so as to evaluate aperture size and projection divergence as a function of tumor size, location and T/NT ratio. We will compare ETACT to SMM and SPECT using these simulated results. We will acquire the cardiac insert for the Data Spectrum phantom. We will develop a methodology for acquiring ETACT data using optical markers. Once developed, we will acquire phantom data that will evaluate fiducial placement, tumor size and location, the effect of cardiac or liver activity and compare the results to SMM and SPECT. In the third year, we will continue to evaluate ETACT through these phantom experiments and will develop a clinical prototype of this method.

References

Grant DG, Tomosynthesis: A three-dimensional radiographic imaging technique. IEEE Trans Biomed Engin 1972; BME-19:20-28.

Webber RL, Horton RA, Tyndall DA, Ludlow JB. Tuned-aperture computed tomography (TACTTM). Theory and application for three-dimensional dento-alveolar imaging. Dentomaxill Radiol 1997; 26:53-62.

Appendix

This appendix includes the figures from the *Body of the Report* as well as the two abstracts listed in the *Reportable Outcomes* section.

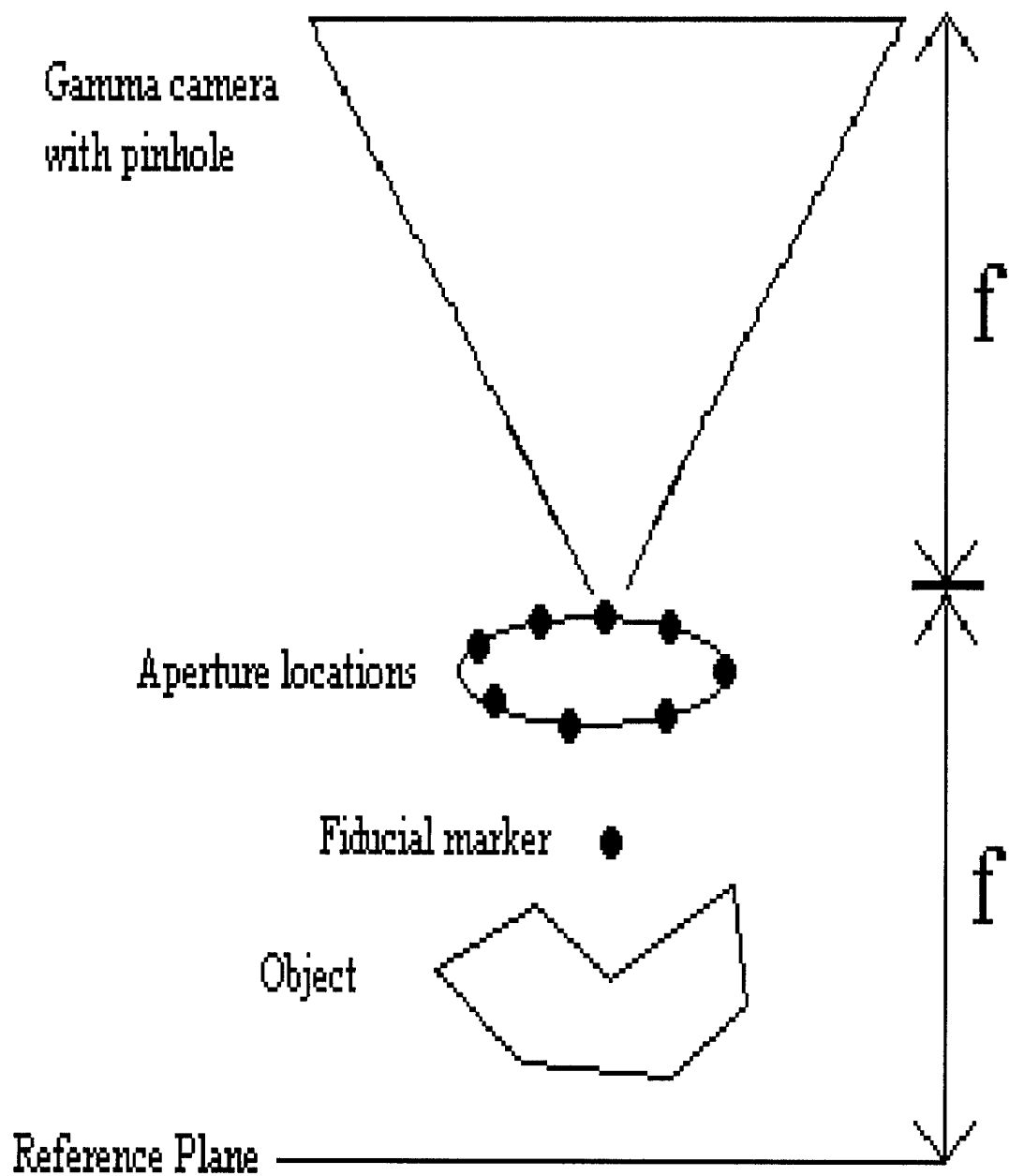


Figure 1. Tomosynthesis. All projections are acquired in the same plane that is parallel to the detector plane. The reference plane is the same distance (f) in front of the aperture as the detector is behind. For ETACT a Fiducial marker is between the aperture and the object.

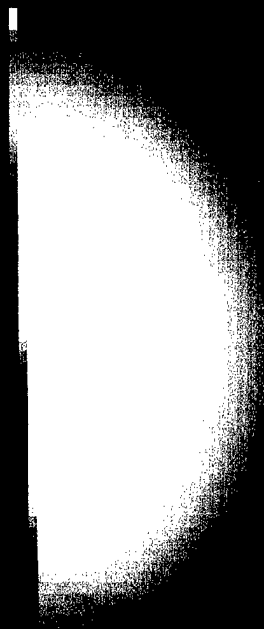


Figure 2. Simulated projection. This projection is prior to blurring and the addition of noise. The tumor (1 cm 5:1 T/NT ratio) is evident as are the 5 markers.

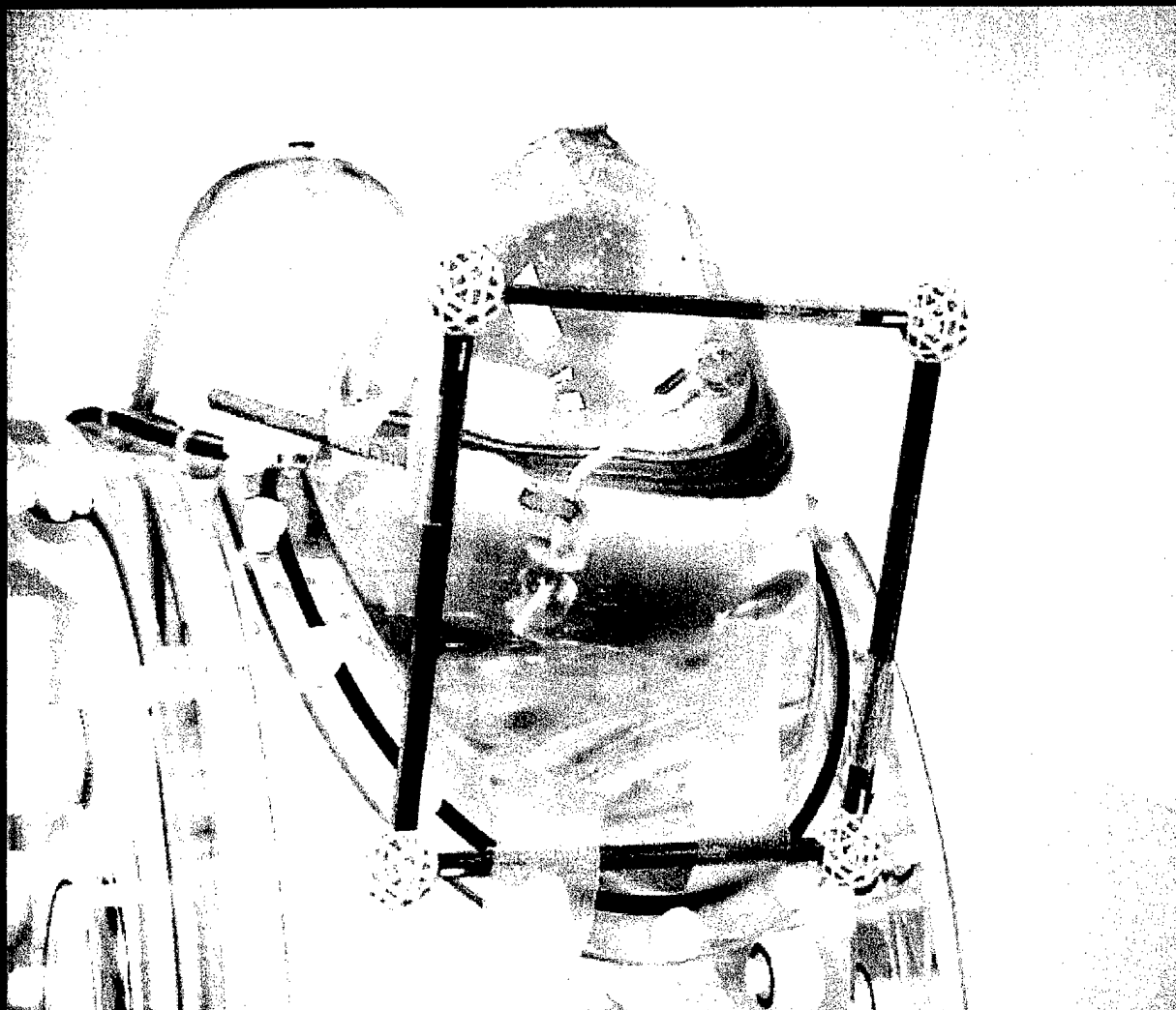


Figure 3. Data Spectrum Breast Phantom. The tumor within the breast is visible. Five markers were used, point sources just inside the the white balls and the 5th one at the end of the red rod.

ETACT Projection Data

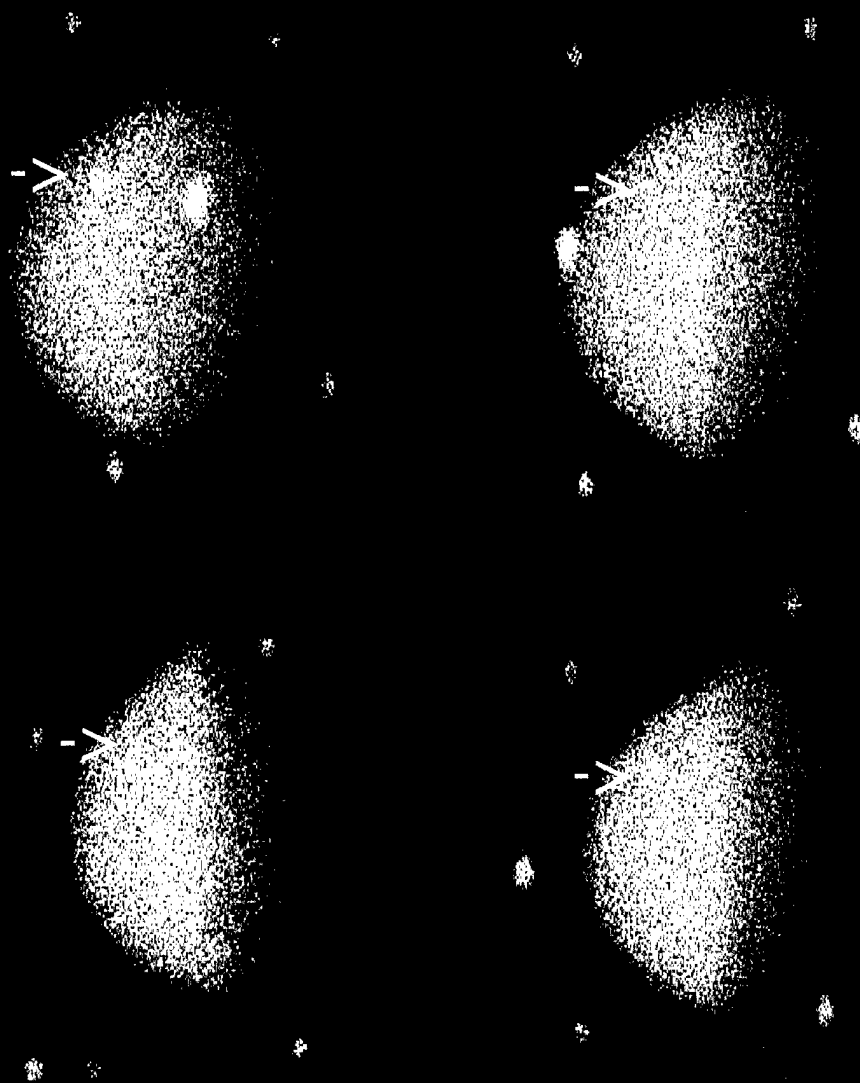


Figure 4. The 5 markers are easily visible on each projection. The tumor is more subtle and is indicated with an arrow on each projection.

ETACT Reconstructed Slices

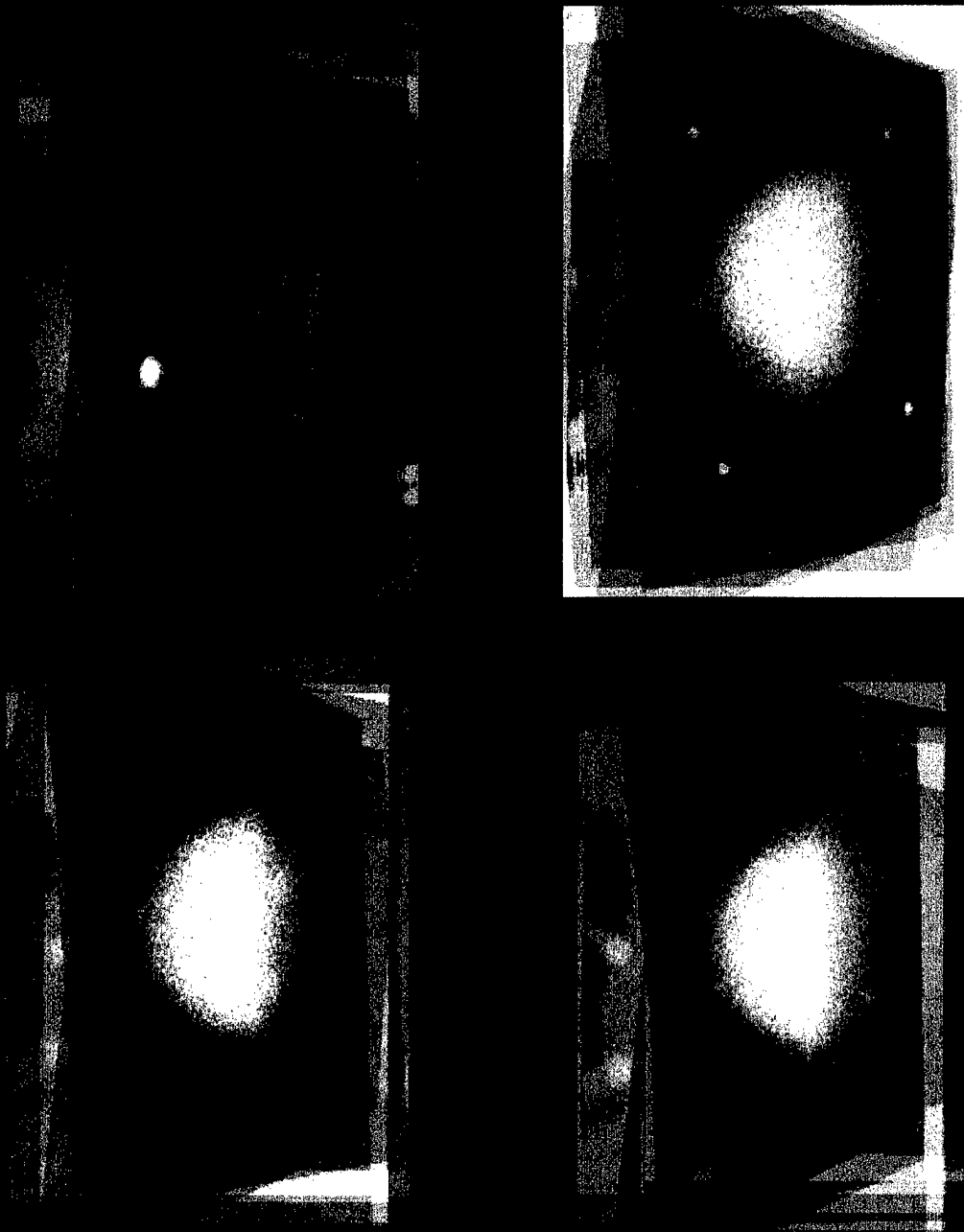


Figure 5. The slice in the upper left is through the Marker at the end of the red rod in Figure 4, the upper Right is through the 4 coplanar markers, the lower left is through the tumor and the lower right is an arbitrary Slice through the breast.

Spatial Resolution and Sensitivity vs Distance

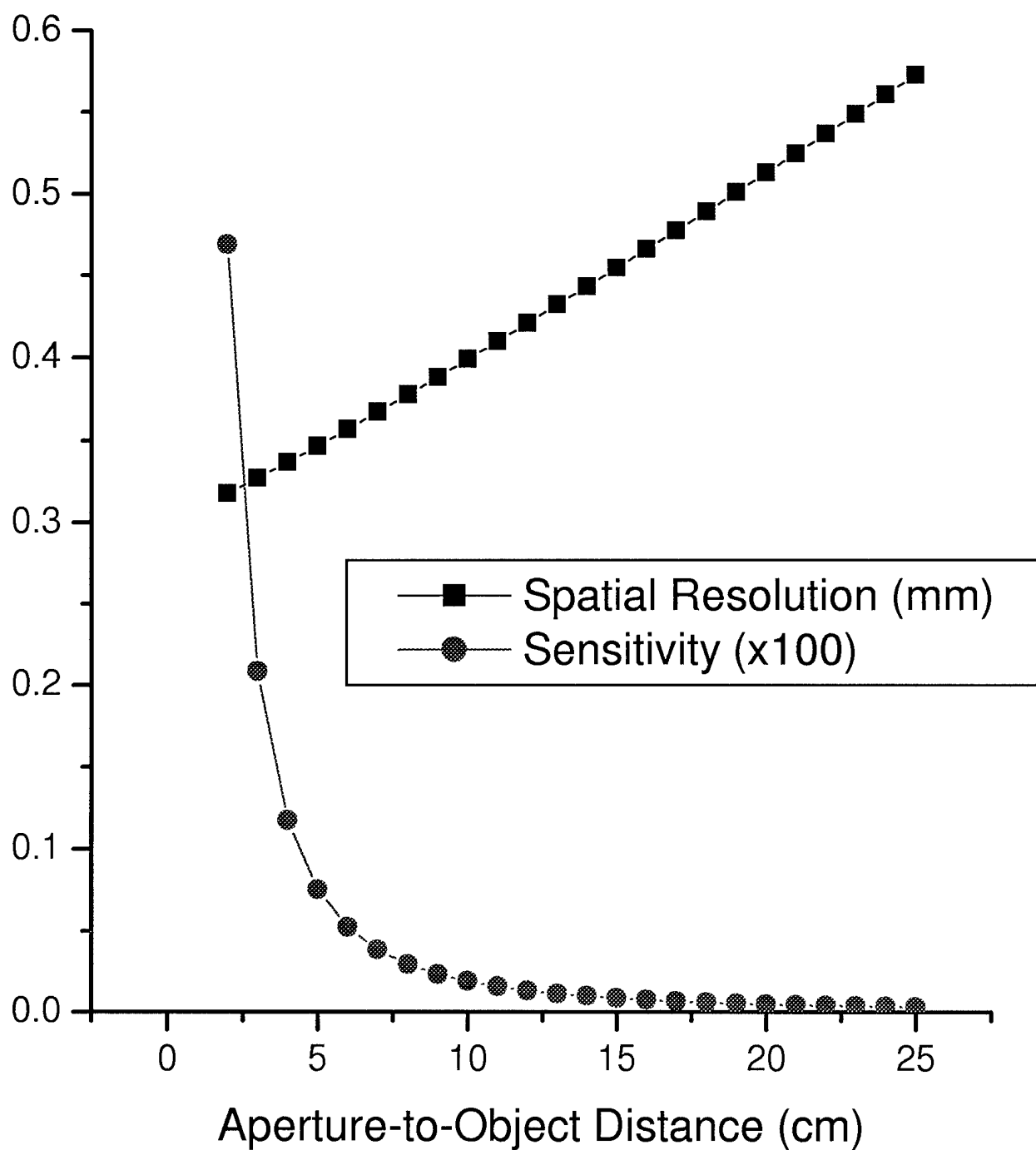


Figure 6. System spatial resolution and sensitivity as a function of aperture to object distance. The aperture size is 3 mm and the intrinsic resolution of the gamma camera is 3.5 mm.

No. 84

ETACT - A NOVEL APPROACH TO SCINTIMAMMOGRAPHY.

* F.H. Fahey, R.L. Webber, B.A. Harkness. Wake Forest University School of Medicine, Winston-Salem, NC

Scintimammography (SMM) using Tc-99m sestimi has very good sensitivity and specificity for lesions that are palpable or greater than 1.5 cm. However, it has limited accuracy with smaller, nonpalpable lesions, mostly due to the limited spatial resolution of planar SMM or the masking presence of radioactivity in other organs such as the heart or liver. Emission tuned aperture computed tomography (ETACT) is a novel yet simple and flexible approach to 3D nuclear imaging that is based on the tuned aperture computed tomography method which has been successfully applied in dental and conventional (x-ray) mammography. A series of projection images of the object, including several fiducial markers, are acquired using a gamma camera with a pinhole collimator. The images can be acquired from any angle provided the entire object and all fiducial markers are in each image. This flexibility allows this method to be applied in a variety of hospital settings (e.g., the mammographic suite) and makes it easier to avoid activity in other organs such as the heart. The data are then reconstructed into a series of tomographic slices. The use of the pinhole collimator leads to an improvement in system spatial resolution compared to planar SMM and reduces the contribution to the image of activity in other organs. The advantage of this approach is that it requires no special hardware, and the reconstruction software can be developed to run on computers readily available in any nuclear medicine clinic. A phantom study was performed to test the method's feasibility. A saline bag (mimicking the breast) was fixed to a cylindrical phantom. The phantom included activity in an insert to simulate cardiac uptake. A 13 mm spherical "tumor" and fiducial markers were added. Five projections were acquired and reconstructed into a series of slices through the object. In this preliminary experiment, the resultant images were of reasonable quality, and the tumor was easily distinguishable from cardiac activity. Although further investigation is required, ETACT is a very promising approach to SMM.

* **Oncology Diagnosis: Breast Lymphoscintigraphy**

2:15PM-3:45PM

Session 13

Room: 714 A/B

Moderator: Naomi Alazraki, MD

Co-Moderator: George H. Hinkle, RPh, MS, BCNP

No. 85

SENTINEL NODE LYMPHATIC MAPPING FOR BREAST CANCER: APPLICATION TO A DIVERSE PATIENT POPULATION

JE Eary, DA Mankoff, LK Dunnwald, D Byrd, B Anderson, R Yeung, R Moe. University of Washington, Seattle, WA

Sentinel lymph node mapping has been investigated as a technique for minimizing the morbidity associated with axillary nodal staging in breast cancer. Most studies published to date have focused on patients presenting with palpable lesions without prior intervention, while in practice, many patients needing axillary staging have had prior surgical biopsy and/or pre-surgical chemotherapy. We therefore performed sentinel lymph node mapping in a population that included patients with prior surgery and/or chemotherapy. A total of 54 patients were mapped using both filtered [Tc-99m]-sulfur colloid lymphoscintigraphy and intraoperative mapping using a radiation probe and visual identification using lymphazurin blue. All patients also underwent a standard axillary nodal dissection after mapping. Eighteen patients had undergone previous excisional biopsy of their lesions, 13 had pre-surgical chemotherapy, 2 had both, and 25 had no prior interventions besides needle biopsy. Eleven patients required ultrasound or mammography localization, while 43 had palpable lesions or biopsy cavities. Lymph mapping successfully identified a sentinel node in 81% of cases, with similar success rates for patients with prior surgery or chemotherapy and patients without prior intervention. The mean time to node visualization in successful cases was 29 minutes (range 2 - 120 minutes), with a mean of 1.4 nodes visualized. At surgery, the sentinel node was identified by radioactivity probing alone in 43% of successful mappings, by blue dye in 7% of cases, and by both in 50% of cases. Twenty-three patients (43%) had one or more positive lymph nodes by pathology, of which 20 had one or more sentinel nodes identified. Sixteen of these patients had a positive sentinel node, while 4 had a negative sentinel node or "skip" lesions (7% of all patients). Three patients with prior chemotherapy (23% of such patients), one patient with prior surgery (6%), and no patients without prior interventions had skip lesions. We conclude that

sentinel node lymphatic mapping for breast cancer is accurate in patients without prior intervention, but must be used with caution in patients with prior interventions.

No. 86

VALUE OF COMBINED IMAGING AND USE OF GAMMA PROBE IN INTRAOPERATIVE LOCALIZATION OF SENTINEL LYMPH NODE IN BREAST CANCER

H. Jadvar, S. Jeffrey, D. Cua, R. Birdwell, H.W. Strauss; Division of Nuclear Medicine and Department of Surgery, Stanford University, Stanford CA

The gamma probe is useful to localize sentinel lymph nodes (SLN) at the time of axillary lymphatic dissection. We studied the value of combined imaging and gamma probe localization of the SLN in 20 patients with breast cancer. Two to four doses of 200 uCi Tc-99m sulfur colloid, each diluted to 1 ml, were injected in the peri-lesion region in all patients. Injection was done around a palpable mass (n=12), in the periphery of excisional biopsy or lumpectomy site guided by sonography (n=6) or guided by mammographic wire localization (n=2). Anterior chest imaging with arms above the head was performed from immediately post injection to up to 4 hours. A Co-57 transmission scan was used for delineation of the body contour. SLN was localized in 12 (60%) patients by imaging and by gamma probe in an additional 7 (35%) patients. Imaging provided unique information regarding drainage toward the internal mammary chain in 3 (15%) patients whose axillary nodal basin were all negative for tumor. The minimum time to visualization was 40 min but most were seen at 2 h. Imaging did not localize the SLN in 8 (40%) patients. Of these 8 patients, 5 were injected in the peri-excisional biopsy or lumpectomy cavity site. The table summarizes the number and the histology of the axillary SLN's that were localized by imaging, gamma probe and isosulfan blue dye for various sites of primary tumor. SLN was not localized by any of the three methods in 1 patient.

	UO (n=11)	LO (n=1)	UI (n=3)	LI (n=2)	Retroareolar (n=3)	Total (n=20)
	I/B/G/H	I/B/G/H	I/B/G/H	I/B/G/H	I/B/G/H	I/B/G/H
Axilla	4/9/9/2	1/1/1/1	0/1/1/0	2/2/2/0	2/3/3/1	9/16/16/4

I=imaging, G=gamma probe, B=isosulfan blue dye, H=histology positive for tumor, UO=upper outer, UI=upper inner, LO=lower outer, LI=lower inner

We conclude that scintigraphic imaging adds significant information to the gamma probe SLN localization. Identification of SLN in the internal mammary chain may avoid the cost and morbidity associated with axillary lymph nodal dissection.

No. 87

LYMPHOSCINTIGRAPHY AND RADIOGUIDED BIOPSY OF THE SENTINEL AXILLARY NODE IN BREAST CANCER. G. Paganelli, C. De Cicco, M. Cremonesi, A. Luini*, M. Bartolomei, C. Grana, G. Prisco, V. Galimberti*, P. Calza, G. Viale***, U. Veronesi*. Divisions of Nuclear Medicine, Senology* and Pathology***. European Institute of Oncology, Milan, Italy

Lymphoscintigraphy (LS) associated with radioguided biopsy of the sentinel node (SN) is well-established in clinical practice for melanoma. In breast cancer the sentinel node concept is similarly valid and lymphoscintigraphy is a useful method for localizing the axillary sentinel node. The aim of the present study was to optimize the LS technique in association with a gamma detecting probe (GDP) for identifying and removing the SN in breast cancer patients.

Methods: Two hundred fifty patients with operable breast tumor underwent LS before surgery. Three different size ranges of ^{99m}Tc-labelled colloid particles (<50, <80, and 200-1000 nm) were used, with either subdermal (above tumor) or peritumoral injection. Early and late scintigraphic images were obtained in anterior and oblique projections, and the skin projection of the detected SN was marked. SNs were identified and removed with the aid of the GDP during breast surgery; they were tagged separately. Complete axillary dissection followed. In 40 patients a blue dye was also administered in addition to subdermal radiolabeled colloid to compare blue dye mapping with LS localization.

Results: LS successfully revealed lymphatic drainage in 245/250 patients (98%). The axillary SN was identified in 240 patients (96%). SN biopsy correctly predicted axillary node status in 234/240 patients (97.5%). LS and GDP detected the SN most easily and consistently when 200-1000 nm colloid was administered subdermally in an injection volume of 0.4 mL. Blue dye mapping was successful in 30/40 patients (75%), in 26 of whom the dye and LS identified the same node; in four cases different nodes were identified. None of these four patients had axillary disease.

Conclusions: LS is a simple procedure that is well-tolerated by patients. SN identification is more reliable when large-size radiolabeled colloids are injected in a relatively small injection volume (0.4ml). Use of a GDP greatly facilitates precise pin-pointing and rapid removal of the SN.

abnormalities. While localized near-surface electrode artifacts have been evident, several findings have emerged. The normal mammogram breast appears to have a characteristic EIS permittivity image emerging across subjects. Structural features in the EIS images have generally correlated with tumors, cysts, scarring from recent lumpectomy and follow-up radiation therapy. We can detect lesions on the order of 1 cm but cannot always precisely locate them. With improved calibration and electrode artifact modeled compensation, we hope to distinguish specific lesions by their absolute conductivity & permittivity values.

MO-E4-05

MRI 3D Contrast Enhanced Acquisition And Phase Contrast Flow Analysis for Internal Mammary Artery Evaluation

Y Liu*, J Blechinger, R Breger, Radiology Dept./St. Luke's Medical Center, Milwaukee, WI

Internal mammary artery (IMA) bypass grafting has been widely used for patients with coronary artery disease. However, stenosis and occlusion of IMA grafts is not uncommon. The purpose of this study is to use contrast enhanced 3D MR angiography for visualization of the IMA, and phase contrast flow analysis for functional evaluation of IMA so that the recurrent cardiac symptoms can be monitored or predicted. Contrast enhanced 3-dimensional (3D) fast gradient echo acquisition is used for patients post IMA graft operation. Forty cc of Gadodiamide contrast is bolus injected in 20 seconds. Images are displayed using maximum intensity projection and reformatting algorithms. To measure the flow of the internal mammary artery, segmented cine phase contrast flow analysis images are acquired. A torso phased array coil is used for the 3D contrast enhanced MRA acquisition. During the followed phase contrast flow analysis acquisition, only the left anterior coil element from the 4 coil element is activated. This approach provides excellent signal during 3D contrast MRA acquisition, while in flow analysis high signal for the left IMA without aliasing artifacts. The IMA is well visualized from its origin at subclavian to left anterior descending coronary anastomosis. Velocity measured from a grafted IMA without stenosis shows biphasic forward flow pattern which is characteristic for IMA graft flow. Combining the 3D contrast enhanced MRA with the phase contrast flow analysis, both morphological and functional evaluation for IMA flow patency can be achieved, so that recurrent cardiac symptoms could be predicted or monitored.

MO-E4-06

* Preliminary Evaluation of ETACT Scintimammography

F Fahey*, R Webber, E Bayram, B Harkness, Z Mu, P Hemler, Wake Forest University School of Medicine, Winston Salem, NC

We have performed a preliminary evaluation of emission tuned aperture computed tomography (ETACT), a novel approach to scintimammography. In ETACT, a series of tomographic slices of the tracer distribution in the breast can be reconstructed from a small number (5-10) of projection images with the use of fiducial markers. The projection data are acquired with a pinhole collimator to take advantage of its high spatial resolution. Projection data are reconstructed tomographically and an iterative axial deconvolution is applied. Computer simulations were performed to investigate the effect of pinhole size on signal-to-noise ratio (SNR). ETACT projections of a computer model of a breast with a 1 cm tumor (5:1 T/NT ratio) were simulated for a 3, 4 and 5 mm pinhole aperture. The use of a 4mm pinhole yielded the optimum contrast and SNR for this particular imaging task ($C = .133, .177, .122$ and $SNR = 1.92, 2.20$ and 2.01 for 3, 4, 5 mm, respectively). ETACT was then performed on the Data Spectrum breast phantom with a 1 cm tumor (10:1 T/NT). Eight projections were acquired with a 4 mm pinhole for 5 min each about the left lateral of the phantom. The ETACT reconstructed data yielded a significant improvement in contrast (0.52 vs 0.20) and SNR (1.85 vs 0.54) relative to planar imaging. These preliminary results indicate that ETACT is a promising new approach to scintimammography.

Refresher Course

Room: Pearl

TU-A1-01

Manpower Issues for Radiation Oncology

Michael Mills, Kenneth Hogstrom¹, Geoffrey Ibbott², University of Louisville, Louisville, KY (1) UT M.D. Anderson Cancer Center, Houston, TX (2) University of Kentucky, Lexington, KY

The emphasis on cost reduction associated with Managed Care continues to burden medical physicists. Radiation oncology managers need to defend levels of staffing and other resources in order to maintain acceptable levels of clinical quality. New and emerging high technologies require the purchase of specialized equipment. The manager must provide for both an initial commissioning effort and an ongoing clinical effort from physicists and dosimetrists. Two comprehensive national surveys measure physics and dosimetry personnel resources associated with radiation oncology. These are The Abt Study of Medical Physics Work Values for Radiation Oncology Physics Services, and the Survey of Physics Resources for Radiation Oncology Special Procedures. The former examines routine radiation oncology procedures. The latter addresses the following special procedures: total body irradiation, total skin irradiation, electron arc therapy, intraoperative radiotherapy, stereotactic radiosurgery, stereotactic brachytherapy, high-dose rate brachytherapy, and three-dimensional treatment planning. These survey data provide a national profile standard for resource management. Effort, equipment and cost are analyzed as a function of number of patients treated with routine and special technologies. The data defends staffing levels, resource management decisions, and the cost benefits of treatment centers becoming referral centers for routine or high technology procedures.

Continuing Education Course Room: Mississippi IMRT - 3

TU-A2-01

IMRT with Conventional MLC's

Lynn Verhey, University of California, San Francisco, CA

The use of three-dimensional conformal radiotherapy (3DCRT) has now become common practice in radiation oncology departments around the world. Typical applications of 3DCRT involve a number of fixed beams entering the patient from directions which are hand-selected with the aid of beams' eye viewing to avoid the traversal of sensitive normal tissues to the maximal extent possible, even if those directions are out of the axial plane. Plan optimization is accomplished iteratively until a satisfactorily uniform dose to the target is achieved without exceeding the dose tolerance of neighboring sensitive tissues.

There remain situations for which conventional 3DCRT cannot produce a satisfactory treatment plan due to limitations of the method along with the geometry of the problem. Intensity modulated radiotherapy (IMRT) uses modifications in the intensity of the beams across the irradiated field as an additional degree of freedom to enhance the capability of conforming dose distributions in three dimensions. There are a number of different methods of producing these intensity-modulated dose distributions, some of which are relatively simple and others quite elegant and complex.

Simple IMRT methods are those which can be planned and iteratively optimized with existing "forward" 3D treatment planning systems. These IMRT plans include fields made up of two or more subfields, shaped with a multileaf collimator (MLC), at least one of which is designed to reduce dose to overlying normal tissues. This planning scheme replaces noncoplanar methods that avoid normal tissue irradiation by complex angle selection alone.

General IMRT methods are those that require the use of inverse treatment planning programs with computerized optimization. These treatments can be accomplished by static "stop and shoot" MLC delivery methods or by dynamic sliding window methods. A significant advantage of the static IMRT method is that each MLC segment is a separate field that can be verified with the accelerator R/V system and that portal verification methods can still be used.